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The Association between Sarcopenia and the Risk of Serious Infection among Adults Undergoing Liver Transplantation

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Abstract

Background—While sarcopenia (muscle loss) is associated with increased mortality after liver transplant, its influence on other complications is less well understood. We examined the association between sarcopenia and the risk of severe post-transplant infections among adult liver transplant recipients.

Methods—We assessed sarcopenia among 207 liver transplant recipients by calculating total psoas area (TPA) on preoperative computed tomography scans. The presence or absence of severe post-transplant infection was determined by review of the medical chart. The influence of post-transplant infection on overall survival was also assessed.

Results—We identified 196 episodes of severe infections among 111 patients. Fifty-six patients had more than one infection. The median time to development of infection was 27 days (range 13–62). When grouped by tertiles, patients in the lowest tertile had a more than four-fold higher odds of developing severe infection compared to patients in the highest tertile; OR 4.6, CI 95 2.3–9.5). In multivariable analysis, recipient age (hazard ratio 1.04, p=0.02), pre-transplant TPA (hazard ratio 0.38, p<0.01) and pre-transplant total bilirubin level (hazard ratio 1.05, p=0.02) were independently associated with the risk of developing severe infections. Patients with severe post-transplant infections had worse 1-year survival compared to patients without infection (76% vs. 92%, p=0.003).

Conclusions—Among patients undergoing liver transplantation, lower TPA was associated with heightened risk for post-transplant infectious complications and mortality. Future efforts should focus on approaches to assess and mitigate vulnerability among patients undergoing transplantation.

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Keywords

Liver Transplantation; Infections; Frailty; Sarcopenia; LT-13-274

INTRODUCTION

Liver transplants are costly and highly morbid procedures. With increased efforts to provide efficient and effective care, much attention has been given to identifying patients that require more intense resource utilization during the perioperative period. One such group of patients is the medically frail. [1–4] Although often thought of as a normal facet of aging, this heightened state of vulnerability (known as "frailty") plays a role in susceptibility to a wide range of illnesses, including infections. [5,6] While there are many proposed ways to establish the presence or absence of frailty, sarcopenia (muscle loss) has gained attention recently due to its reproducibility and its demonstrated link with increased mortality and morbidity risk across diverse patient groups. [7–10]

While the influence of sarcopenia on the overall health of older adults has been well recognized, the potential impact of frailty on surgical outcomes has only recently generated interest. Sarcopenia has been used to evaluate perioperative risk across several patient populations. Sarcopenic patients appear to be at increased risk of major postoperative complications and death following a variety of surgical procedures including liver transplantation.[11–14]

Previously, we described the relationship between sarcopenia and post-liver transplant survival. [15] Although we observed a robust association between sarcopenia and increased mortality, other clinical outcomes of interest were not considered. Improved understanding of the influence of sarcopenia on post-transplant risk can inform the development of better management strategies for this vulnerable population. In that context, we examined the relationship between sarcopenia and infectious complications following liver transplantation.

METHODS

Setting and study population

The University of Michigan Health System (UMHS) is a 931-bed, tertiary care medical center with an active liver transplantation program. The UMHS liver transplant program began in 1985 and now performs both pediatric and adult liver transplants. Our study population included all adult patients that underwent liver transplantation between June 2002 and August 2008 and also underwent preoperative abdominal/pelvic computed tomography (CT) scan during the 90 days prior to transplantation.

Outcomes

The development of severe infections (primarily healthcare-associated and opportunistic infections) within 180 days of transplantation was the primary outcome of interest. The presence or absence of infection and associated organism(s) were determined by review of recipients' medical records. We defined severe infections as those requiring hospitalization, intravenous or prolonged courses of antimicrobials or infections resulting in persistent disability or death. We focused on severe infections as more minor infections (mild cellulitis, uncomplicated urinary tract infection, etc) are generally of limited clinical consequence. We defined healthcare-associated infections and opportunistic infections using established Centers for Disease Control and Prevention/National Healthcare Safety Network and American Society of Transplantation criteria. [16,17] From a practical standpoint, minor

infections are also nearly impossible to ascertain in a retrospective manner. We recorded time to diagnosis of infection and mortality as secondary outcomes.

Independent variables

Our primary exposure of interest was sarcopenia, measured by patient total psoas area (TPA). We computed each patient's TPA from preoperative abdominal/pelvic CT scans as previously described. [15] In brief, we calculated the cross-sectional area of both psoas muscles at the level of the fourth lumbar vertebra via a standardized computer algorithm. Other patient characteristics were recorded including demographics, height, weight, body mass index (BMI), indication for liver transplant, preoperative laboratory values, and presence of portal vein thrombosis. Preoperative laboratory values were used to calculate patient model for end-stage liver disease (MELD) scores.

Statistical Analysis

To account for known gender influences on TPA in our analysis, we first grouped patients into gender-stratified TPA tertiles, so that each tertile contained similar proportions of men and women. [9,18] We then compared patient demographics, preoperative characteristics, preoperative lab values and donor characteristics across TPA tertiles using one-way analysis of variance to compare continuous variables and Pearson chi-squared tests to compare categorical variables. We included all transplant indications when comparing indications across TPA tertiles. Next, we compared patient demographics, characteristics, lab values and donor characteristics across groups by the presence of severe post-transplant infection using unpaired t-tests for continuous variables and Pearson chi-squared tests or Fisher's exact test for categorical variables. When comparing groups according to infection, we only considered each patient's primary indication for transplant if they had multiple indications. We further categorized primary transplant indications into one of three categories (hepatocellular carcinoma without hepatitis C virus infection, hepatitis C Virus, and 'other') for bivariate analysis and further modeling.

To examine the relationship between TPA and post-transplant severe infection, we first used logistic regression to calculate the unadjusted odds ratio (OR) for developing severe infections by TPA tertile level. We then entered all variables with p-values less than <0.2 in univariate analysis into a used Cox proportional hazards regression with backwards-stepwise selection to identify independent risk factors for developing severe post-transplant infection. We examined risk factors for developing bacterial, fungal or viral infections using the same method.

For survival analysis, we calculated the days from transplantation to death. We elected to censor survival at the end of the study period or last date of follow-up, whichever occurred first. We estimated survival functions using the Kaplan-Meier method, stratifying patients across presence of severe infection. Finally, we compared survival curves and 1-year survival rates between groups (infected or not infected) using the log-rank test.

We considered a two-tailed p-value of less than 0.05 to be significant. All statistical analyses were performed using used SAS 9.2 (SAS Institute; Cary, NC). This study was approved by the University of Michigan Institutional Review Board.

RESULTS

Patient Characteristics

Between June 2002 and August 2008, 509 adult patients underwent liver transplantation at UMHS. Of these, 207 (40.7%) underwent abdominal CT scanning within the 90 days prior

to transplant. These 207 patients formed our overall study cohort. The mean age among the cohort was 51.7 ± 9.8 years; 129 patients (62.3%) were male. The majority of patients (81.2%) were white. The most frequent indications for transplant were hepatitis C virus (26.1%), hepatocellular carcinoma (HCC) (25.1%), and alcoholic cirrhosis (14.5%). Ten patients (Forty-nine patients had more than one indication for transplant.

Patient characteristics across TPA tertiles are presented in Table 1. Compared to patients with low TPA, patients with high TPA had higher mean BMI (29.3 kg/m^2 vs. 26.5,kg/m^2 p=0.03), were more likely to have a diagnosis of hepatocellular carcinoma (HCC) (37.7% vs. 14.5%, p=0.01), and had lower mean MELD scores (18.0 vs. 22.7 p<0.01) (Table 1).

Table 2 shows differences between patients who developed severe post-transplant infections and those who did not. Compared to patients who did not have a severe infection, infected patients had higher mean MELD scores (21.8 vs. 17.4, p<0.01), lower mean albumin levels (2.7 g/dL vs. 2.9 g/dL, p=0.04), and lower TPA (1762 mm^2 vs. 2116 mm^2, p<0.01). In addition, infection patients were less likely to have HCC as an indication for transplant (15.3% vs 36.5%, p<0.01) (Table 2). Overall, patients with severe post-transplant infections had higher mortality (36.0%) than patients without infection (18.8%, p<0.01).

Post-Transplant Infections

We identified 196 severe infectious episodes among 111 patients. Fifty-six patients had more than one infection. The median time to the first infectious episode was 27 days (interquartile range 13–62); 53.1% of infections occurred within 30 days of transplant and73.9% occurred with 60 days of transplant.

The most common infectious episodes were bloodstream infections (n=48), intra-abdominal infections (n=65), and pneumonia (n=14). In addition, there were 15 opportunistic infections, of which the majority (60.0%) were related to cytomegalovirus. Details on the types of infections and associated microorganisms are display in Table 3.

Risk factors for developing severe post-transplant infections

As shown in Table 4, decreasing TPA (more sarcopenia) was associated with increased odds of developing any infection (odds ratio (OR) for TPA tertile 1 vs. tertile 3, 4.6, 95% CI 2.3–9.5) or any bacterial infection (OR for TPA tertile 1 vs tertile 3, 5.2, 95% CI 2.5–10.8, also OR for TPA tertile 2 vs tertile 3, 2.5, 95% CI 1.2–5.1). The results of multivariable Cox proportional hazard regression are presented in Table 5. We identified the following variables as independent risk factors for developing a serious infection: recipient age (hazard ratio [HR] for developing any infection 1.04, p=0.02), pre-transplant TPA (HR for increasing TPA tertile 0.38, p<0.01) and pre-transplant total bilirubin level (HR 1.05, p=0.02) (Table 5). Each of these factors remained statistically significant when stratifying infectious episodes by pathogen type (bacterial, fungal or viral).

Survival

Fifty-eight patients died during the study period. Patients with severe infections had more than a twice the odds of post-transplant mortality than patients without infections (OR 2.4, 95% CI 1.3–4.6). The survival curves for patients with and without a severe post-transplant infection are displayed in Figure 1. Patients with any infection had lower 1-year survival (76% vs 92% for patients without infection, p=0.003; log-rank test).

DISCUSSION

The need for evidence-based methods to reduce perioperative risk among vulnerable populations remains critical. These issues continue to garner much attention from policy-makers and medical leaders. [19] Sarcopenia is a reproducible marker of vulnerability and is closely linked to increased mortality and morbidity risk across diverse patient and procedure groups. The preceding results suggest that pre-transplant sarcopenia, measured by TPA, is associated with increased risk of serious post-transplant infections among a cohort of patients undergoing liver transplantation. In addition, we observed that patients with severe post-transplant infections had decreased survival compared to recipients without infections.

This work adds to a growing body of literature highlighting the negative influence of sarcopenia on patient outcomes. Previous research suggests that frailty in general and sarcopenia in particular is associated with poor outcomes following stroke, hip fracture, and both elective and cancer operations. [4,11–13,20] Although we used TPA to quantify sarcopenia, the use of other frailty measures demonstrate similar outcomes. For example, Kaido and colleagues used bioelectrical impedance analysis to assess sarcopenia in a cohort of 124 adult patients undergoing living donor liver transplantation.[14] Their findings mirror our results; low skeletal muscle mass was independently associated with post-transplant mortality.

Our findings are novel in the demonstration of an association between sarcopenia and an increased risk of infectious complications after liver transplantation. Infectious complications are significant sources of morbidity and mortality for liver transplant recipients; the potential influence of sarcopenia on infection-related outcomes deserves further investigation. [21] Improving our understanding of how sarcopenia contributes to an individual patient's risk and subsequent outcomes will be fundamental to developing effective countermeasures for risk reduction and management.

Some investigators have suggested that preoperative risk stratification to identify patients with the highest risk can help inform patient conversations and enact more intensive preoperative preparation, sometimes called "prehabilitation." [22–25] Among patients awaiting liver transplantation, this may not be feasible given the sporadic nature of organ availability and poor overall health of transplant candidates. An alternative strategy may be to use measures of frailty such as sarcopenia to preemptively identify patients for more intensive postoperative monitoring and care—specifically related to infection. Such measures might include using different peri-operative antimicrobial regimens or approaches to infection prophylaxis, early intensive care unit transfer for sarcopenic patients who experience complications, or extra vigilance in terms of removing lines and devices as soon as possible. Further investigation should help clarify which management strategies would be most efficacious to mitigate or manage these patients' increased morbidity and mortality risk.

Our study has several important limitations. First, we analyzed a relatively small cohort from a single transplant center. Future studies should include larger numbers of patients from multiple institutions using prospectively recorded data. In addition, we only assessed liver transplant candidates who had preoperative abdominal/pelvic CT scans, which could result in a selection bias since patients who did and did not have a preoperative CT scan may be inherently different. As such, our results may not apply to a broader liver transplant recipient population. We did not attempt to investigate differences in microbiology or site of infection across TPA levels or the potential effect of antimicrobial treatment. Of note, all patients received standard perioperative infection prophylaxis consisting of ampicillin/sulbactam or vancomycin/levofloxacin (in the setting of penicillin allergy). We also did not account for the potential impact of pre-transplant infections or more minor post-operative

infections. Other clinical factors such as immunosuppression regimens were also not considered, although at least initially, most patients received similar regimens with our standard protocol including steroid induction, tacrolimus, mycophenlate, and steroid maintenance, followed by a reducation in the steroid dose over approximately three months. Finally, there is a possible ascertainment bias for infections that might have occurred outside of UMHS (and not reported).

While the association between sarcopenia, infection and mortality was striking, we cannot infer causality from these results. Nonetheless, the mechanism is biologically plausible, and this work lends additional support for the importance of frailty on outcomes after liver transplantation. Further work should examine other potential mechanisms for increased mortality among sarcopenic patients as well as factors that may have confounded these results. Finally, while sarcopenia is a consistent marker of increased risk, it remains unclear whether it can be mitigated or improved, especially in a population as ill as our study cohort.

Sarcopenia, measured by TPA, seems to provide a convenient and relatively simple means to assess a patient's physiologic reserve and may identify those at increased risk for post-transplant complications and mortality. Specifically, those patients with smaller TPA seem to be at higher risk of developing severe infections. Besides larger confirmatory studies, there is a critical need to better understand how best to assess and mitigate vulnerability in this extremely high-risk patient population, remains critical.

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ABBREVIATIONS

BMI	body mass index
CMV	cytomegalovirus
CT	computed tomography
HCC	hepatocellular carcinoma
HCV	hepatitis c virus
HR	hazard ratio
INR	international normalized ratio
MELD	Model for End-stage Liver Disease
OR	odds ratio
TPA	total psoas area
UMHS	University of Michigan Health System

References

1. Buchman AS, Wilson RS, Bienias JL, Bennett DA. Change in Frailty and Risk of Death in Older Persons. Exp Aging Res. 2009; 35:61–82. [PubMed: 19173102]
2. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in Older Adults: Evidence for a Phenotype. J Gerontol A Biol Sci Med Sci. 2001; 56:M146–56. [PubMed: 11253156]

3. Lang PO, Michel JP, Zekry D. Frailty Syndrome: A Transitional State in a Dynamic Process. Gerontology. 2009; 55:539–549. [PubMed: 19346741]
4. Makary MA, Segev DL, Pronovost PJ, Syin D, Bandeen-Roche K, Patel P, et al. Frailty as a Predictor of Surgical Outcomes in Older Patients. J Am Coll Surg. 2010; 210:901–908. [PubMed: 20510798]
5. Wong CH, Weiss D, Sourial N, Karunananthan S, Quail JM, Wolfson C, et al. Frailty and its Association with Disability and Comorbidity in a Community-Dwelling Sample of Seniors in Montreal: A Cross-Sectional Study. Aging Clin Exp Res. 2010; 22:54–62. [PubMed: 19940555]
6. Woods NF, LaCroix AZ, Gray SL, Aragaki A, Cochrane BB, Brunner RL, et al. Frailty: Emergence and Consequences in Women Aged 65 and Older in the Women's Health Initiative Observational Study. J Am Geriatr Soc. 2005; 53:1321–1330. [PubMed: 16078957]
7. Fielding RA, Vellas B, Evans WJ, Bhasin S, Morley JE, Newman AB, et al. Sarcopenia: An Undiagnosed Condition in Older Adults. Current Consensus Definition: Prevalence, Etiology, and Consequences. International Working Group on Sarcopenia. J Am Med Dir Assoc. 2011; 12:249–256. [PubMed: 21527165]
8. Lang T, Streeper T, Cawthon P, Baldwin K, Taaffe DR, Harris TB. Sarcopenia: Etiology, Clinical Consequences, Intervention, and Assessment. Osteoporos Int. 2010; 21:543–559. [PubMed: 19779761]
9. Iannuzzi-Sucich M, Prestwood KM, Kenny AM. Prevalence of Sarcopenia and Predictors of Skeletal Muscle Mass in Healthy, Older Men and Women. J Gerontol A Biol Sci Med Sci. 2002; 57:M772–7. [PubMed: 12456735]
10. Marcell TJ. Sarcopenia: Causes, Consequences, and Preventions. J Gerontol A Biol Sci Med Sci. 2003; 58:M911–6. [PubMed: 14570858]
11. Tosteson AN, Gottlieb DJ, Radley DC, Fisher ES, Melton LJ 3rd. Excess Mortality Following Hip Fracture: The Role of Underlying Health Status. Osteoporos Int. 2007; 18:1463–1472. [PubMed: 17726622]
12. Peng PD, van Vledder MG, Tsai S, de Jong MC, Makary M, Ng J, et al. Sarcopenia Negatively Impacts Short-Term Outcomes in Patients Undergoing Hepatic Resection for Colorectal Liver Metastasis. HPB (Oxford). 2011; 13:439–446. [PubMed: 21689226]
13. Peng P, Hyder O, Firoozmand A, Kneuertz P, Schulick RD, Huang D, et al. Impact of Sarcopenia on Outcomes Following Resection of Pancreatic Adenocarcinoma. J Gastrointest Surg. 2012; 16:1478–1486. [PubMed: 22692586]
14. Kaido T, Ogawa K, Fujimoto Y, Ogura Y, Hata K, Ito T, et al. Impact of Sarcopenia on Survival in Patients Undergoing Living Donor Liver Transplantation. Am J Transplant. 2013
15. Englesbe MJ, Patel SP, He K, Lynch RJ, Schaubel DE, Harbaugh C, et al. Sarcopenia and Mortality After Liver Transplantation. J Am Coll Surg. 2010; 211:271–278. [PubMed: 20670867]
16. Division of Healthcare Quality Promotion National Center for Emerging, Zoonotic and Infectious Diseases. The National Healthcare Safety Network (NHSN) Manual: Patient Safety Component (PSC) Manual. Atlanta, GA: Centers for Disease Control and Prevention; 2013. CDC/NHSN Surveillance Definition of Healthcare-Associated Infection and Criteria for Specific Types of Infections in the Acute Care Setting; p. 17-1.
17. Humar A, Michaels M. AST ID Working Group on Infectious Disease Monitoring. American Society of Transplantation Recommendations for Screening, Monitoring and Reporting of Infectious Complications in Immunosuppression Trials in Recipients of Organ Transplantation. Am J Transplant. 2006; 6:262–274. [PubMed: 16426310]
18. Melton LJ 3rd, Khosla S, Crowson CS, O'Connor MK, O'Fallon WM, Riggs BL. Epidemiology of Sarcopenia. J Am Geriatr Soc. 2000; 48:625–630. [PubMed: 10855597]
19. Chow, WB.; Ko, CY.; Rosenthal, RA.; Esnaola, NF. ACS NSQIP/AGS Best Practice Guidelines : Optimal Preoperative Assessment of the Geriatric Surgical Patient. 2012.
20. Longstreth WT Jr, Bernick C, Fitzpatrick A, Cushman M, Knepper L, Lima J, et al. Frequency and Predictors of Stroke Death in 5,888 Participants in the Cardiovascular Health Study. Neurology. 2001; 56:368–375. [PubMed: 11171903]

21. Jain A, Reyes J, Kashyap R, Dodson SF, Demetris AJ, Ruppert K, et al. Long-Term Survival After Liver Transplantation in 4,000 Consecutive Patients at a Single Center. Ann Surg. 2000; 232:490–500. [PubMed: 10998647]

22. Brown K, Topp R, Brosky JA, Lajoie AS. Prehabilitation and Quality of Life Three Months After Total Knee Arthroplasty: A Pilot Study. Percept Mot Skills. 2012; 115:765–774. [PubMed: 23409591]

23. Carli F, Charlebois P, Stein B, Feldman L, Zavorsky G, Kim DJ, et al. Randomized Clinical Trial of Prehabilitation in Colorectal Surgery. Br J Surg. 2010; 97:1187–1197. [PubMed: 20602503]

24. Mayo NE, Feldman L, Scott S, Zavorsky G, Kim do J, Charlebois P, et al. Impact of Preoperative Change in Physical Function on Postoperative Recovery: Argument Supporting Prehabilitation for Colorectal Surgery. Surgery. 2011; 150:505–514. [PubMed: 21878237]

25. Malani PN. Functional Status Assessment in the Preoperative Evaluation of Older Adults. JAMA. 2009; 302:1582–1583. [PubMed: 19826029]

Table 1

Characteristics of liver transplant recipients at the University of Michigan Health System from June 2002 to July 2008 with preoperative computed tomography scans stratified by total psoas area tertiles (N = 207)

Characteristic	Tertile 1 (n= 69)	Tertile 2 (n = 69)	Tertile 3 (n = 69)	p-value
Age at transplant (y, mean ± SD)	52.0 ± 9.8	52.0 ± 10.2	51.1 ± 9.6	0.82
TPA, male (mm^2, mean ± SD)	1499.2 ± 309.9	2224.8 ± 157.8	2915.7 ± 381.5	<0.01
TPA, female (mm^2, mean ± SD)	954.3 ± 225.3	1423.1 ± 120.5	1978.8 ± 282.0	<0.01
Race (n, %)				
White	53 (76.8)	61 (88.4)	54 (78.3)	0.17
African American	5 (7.2)	7 (10.1)	11 (15.9)	0.30
Preoperative BMI (mean ± SD)	26.5 ± 5.6	27.5 ± 6.4	29.3 ± 6.3	0.03
Indications for Transplantation* (n, %)				
Hepatitis C virus	22 (31.9)	19 (27.5)	13 (18.8)	0.21
Hepatitis B virus	2 (2.9)	2 (2.9)	5 (7.3)	0.35
Hepatocellular carcinoma	10 (14.5)	16 (23.2)	26 (37.7)	0.01
Alcoholic cirrhosis	11 (15.6)	11 (15.6)	8 (11.6)	0.70
Primary sclerosing cholangitis	6 (8.7)	5 (7.3)	10 (14.5)	0.33
Primary biliary cirrhosis	6 (8.7)	4 (5.8)	5 (7.3)	0.81
Autoimmune hepatitis	4 (5.8)	3 (4.4)	4 (5.8)	0.91
Nonalcoholic steatohepatitis	2 (2.9)	3 (4.4)	3 (4.4)	0.88
Fulminant hepatitis failure	1 (1.5)	2 (2.9)	1 (1.5)	0.78
Alpha-1 antitrypsin deficiency	1 (1.5)	2 (2.9)	0	0.36
Wilson's disease	0	1 (1.5)	1 (1.5)	0.60
Other	9 (13.0)	6 (8.7)	4 (5.8)	0.33
Need for pre-transplant dialysis	6 (8.7)	1 (1.5)	3 (4.4)	0.13
Preoperative lab values (mean ± SD)				
MELD score	22.7 ± 7.9	18.7 ± 8.2	18.0 ± 6.2	<0.01
INR	1.6 ± 0.7	1.5 ± 1.0	1.5 ± 0.4	0.15
Creatinine (mg/dL)	1.9 ±1.3	1.3 ± 0.9	1.2 ± 0.7	<0.01
Total bilirubin (mg/dL)	4.2	4.0	3.2	0.44
Donor age (years, mean ± SD)	42.2 ± 18.0	36.6 ± 17.2	39.7 ± 15.6	0.17

*Numbers reported as total number of diagnoses.

49 patients had more than one indication for transplant. Hepatitis C infected patients are divided by the presence or absence of hepatocellular carcinoma (HCC)

TPA: Total Psoas Area measured at the 4^{th} lumbar vertebrae; BMI: body mass index; MELD: model for end stage liver disease; INR: International normalized ratio

Table 2

Characteristics of liver transplant recipients with and without infection.

Characteristic	Infection (N = 111)	No Infection (N = 96)	p value
Age at transplant (years, Mean ± SD)	52.3 ± 8.8	50.9 ± 10.8	0.30
Male (N, %)	64 (57.7)	65 (67.7)	0.14
Race (N, %)			
White	91 (82.0)	77 (80.2)	0.75
African American	11 (9.9)	12 (12.5)	0.66
Indication for Transplant* (N, %)			
HCV without HCC	34 (30.6)	20 (20.8)	0.11
HCC	17 (15.3)	35 (36.5)	<0.01
Other	60 (54.1)	41 (42.7)	0.10
Need for pre-transplant dialysis	8 (7.2)	2 (2.1)	0.11
Preoperative laboratory values (Mean ± SD)			
MELD score	21.8 ±7.8	17.4 ± 6.9	<0.01
INR	1.6 ± 0.6	1.6 ± 0.9	0.91
Creatinine mg/dL	1.7 ±1.2	1.2 ± 0.7	<0.01
Total bilirubin mg/dL	7.6 ± 8.5	4.9 ± 6.6	<0.01
Serum albumin g/dL	2.7 ± 0.6	2.9 ± 0.7	0.04
BMI (kg/m^2, Mean ± SD)	28.0 ± 5.7	27.5 ± 6.7	0.56
TPA (mm^2, Mean ± SD)	1762.4 ± 701	2116 ± 643.3	<0.01
Donor age (years)	40.4 ± 17.2	38.4 ± 16.8	0.43
Portal vein thrombosis (N, %)	3 (3.1)	7 (6.3)	0.35
Mortality (N, %)	40 (36.0)	18 (18.8)	<0.01

*Numbers indicate primary indication for transplant as recorded in the patient chart. Patients with multiple indications for transplant were assigned a primary for bivariate analysis

BMI: body mass index; TPA: Total Psoas Area measured at the 4^{th} lumbar vertebrae; MELD: model for end stage liver disease; INR: International normalized rato

Table 3

Microorganisms associated with severe infections among patients undergoing liver transplantation

TYPE OF INFECTION	N
Bloodstream/CLABSI (n=48)	
Staphylococcus aureus	5
Coagulase negative Staphylococcus	6
Enterococcus faecalis	5
Vancomycin-resistant *Enterococcus*	6
Morganella morgani	1
Pseudomonas aeroginosa	3
Escherichia coli	3
Klebsiella pneumoniae	2
Candida albicans	5
Candida glabrata	5
Alpha-hemolytic Streptococcus	1
Streptococcus milleri	1
Serratia maltophilia	1
Polymicrobial	4
Intra-abdominal Infection (n=65)	
Staphylococcus aureus	3
Vancomycin-sensitive *Enterococcus*	6
Vancomycin-resistant *Enterococcus*	14
Alpha-hemolytic Streptococcus	1
Pseudomonas aeroginosa	3
Klebsiella oxytoca	2
Klebsiella pneumoniae	2
Candida albicans	2
Candida glabrata	3
Polymicrobial	22
No organism isolated	7
Surgical site infection (n=9)	
Stapylococcus aureus	3
Escherichia coli	1
Enterobacter cloacae	1
Polymicrobial	2
No organism isolated	2
Pneumonia (n=14)	
Pseudomonas aeruginosa	4
Klebsiella oxytoca	1
Candida glabrata	1
Polymicrobial	*2*
No organism isolated	6

TYPE OF INFECTION	N
Urinary Tract Infection (n=8)	
Vancomycin-resistant Enterococcus	2
Escherichia coli	2
Klebsiella pneumoniae	2
Enterobacter species	1
Polymicrobial	1
Colitis (n=31)	
Clostridium difficile	30
Klebsiella pneumonia	1
Opportunistic infection (n=15)	
Epstein-Barr virus	1
Cytomegalovirus (CMV) infections*	9
Disseminated histoplasmosis	1
Cryptococcus peritonitis	1
Cryptococcus fungemia	1
Aspergillus pneumonia	1
Aspergillus osteomyelitis	1
Other (n=6)	
St. Louis Encephalitis virus	1
Cutaneous Herpes Simplex	2
Herpes Zoster	2
Influenza A virus	1

* CMV infections included: CMV colitis (4), CMV hepatitis (1), and disseminated CMV infection (4)

TABLE 4

Unadjusted odds ratios for developing any serious infection after liver transplantation by total psoas areas (TPA) tertiles

	Odds ratio for developing a severe infection after transplant (95% CI)			
TPA Tertiles	**Any infection**	**Bacterial infection**	**Fungal infection**	**Viral infection**
1st vs 3rd Tertile	4.6 (2.25,9.53)	5.2 (2.53,10.8)	2.8 (0.82,9.25)	0.70 (0.21,2.30)
2nd vs 3rd Tertile	1.9 (0.97,3.80)	2.5 (1.25,5.09)	1.5 (0.42,5.75)	0.70 (0.21,2.30)

TABLE 5

Multivariable analysis of pre-operative risk factors associated with the development of a severe infection after liver transplantation (n=207 patients). Results are presented for all infections “Any Infection” as well as subsets of “Bacterial”, “Fungal” and “Viral” pathogens. Details are provided in Table 3.

	Hazard ratio for developing a severe infection after transplant (95% CI)			
VARIABLE	**ANY INFECTION**	**BACTERIAL INFECTION**	**FUNGAL INFECTION**	**VIRAL INFECTION**
Age at transplantation	1.04* (1.01,1.08)	1.04* (1.01,1.08)	1.04* (1.01,1.08)	1.04* (1.01,1.08)
Body Mass Index	1.04 (0.99,1.08)	1.04 (0.99,1.08)	1.04 (1.00,1.09)	1.03 (0.99,1.08
Pre-transplant serum creatinine	0.84 (0.61,1.13)	0.83 (0.61, 1.13)	0.86 (0.64,1.17)	0.88 (0.65,1.19)
Pre-transplant Total Bilibrubin	1.05* (1.01,1.10)	1.05* (1.00,1.09)	1.05* (1.00,1.09)	1.05* (1.01,1.09)
Pre-operative total psoas area	0.38* (0.23,0.65)	0.38* (0.23,0.65)	0.35* (0.21,0.59)	0.34* (0.20,0.58)
Pre-operative MELD score	0.99 (0.93,1.05)	0.99 (0.94,1.05)	0.99 (0.94,1.05)	0.99 (0.94,1.05)

* $p<0.05$

MELD: model for end stage liver disease